Solvent Effects on Molecular Interactions in 2-Amino- and 3-Amino-pyridine–Molecular Iodine–Solvent Systems

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Equilibria in 2-amino- and 3-amino-pyridine–molecular iodine–solvent (cyclohexane, carbon tetrachloride, benzene, or chlorobenzene) systems have been studied by electronic spectroscopy. The heats of solution (ΔH_s) of the amines and the heats of complexation with I_2 (ΔH_c) have been measured by a calorimetric method. The results have been interpreted in terms of the solvent dependence of the ΔG_c, ΔH_c, and ΔH_s values obtained, and compared with data for other pyridine derivative–I_2–solvent systems.

Pyridine derivative–iodine complexes have been studied by a number of investigators;[1,2] most of the work, however, has been done with donors of medium basicity (pK_a < 6), studied in only one solvent, with the aim of testing Mulliken's theory or free energy correlations (ΔG_c or spectral shift *vs.* pK_a of the amine). More basic donors are, as a rule, avoided because they are likely to form ionic complexes, especially in the presence of traces of water or other impurities.[3]

We have previously studied solvent effects on the interactions of alkyl- and chloro-substituted pyridines and quinolines with molecular iodine.[2,4] We now report results obtained for comparatively strong donors of the pyridine series, differing in steric properties, *viz.* 2-amino- and 3-amino-pyridine (pK_a 6.71 and 6.03, respectively); we wished to investigate how the presence of two donor sites in the base would modify the complexation and solvation patterns revealed by the systems previously studied. Only spectroscopic data can be found in the literature[5] for the aminopyridine–I_2 systems, and these are not correlated with solvent effects.

Experimental

Reagents.—Solvents and iodine were purified as previously described.[2] 2-Aminopyridine (2-APy) (pure; Roanal, Budapest) and 3-aminopyridine (3-APy) (pure; Schuchardt, München) were recrystallized from benzene–hexane.[6] All preparative operations were performed in a dry-box.

Spectrophotometric Measurements.—These were performed with a Beckman u.v. 5270 spectrophotometer for solutions in thermostatted (±0.1 K) stoppered quartz cells.

Calorimetric Measurements.—The enthalpies of complex formation, ΔH_c, of solution, ΔH_s, and of dilution, ΔH_d, were determined under moisture-free conditions by using a 'constant temperature environment' calorimeter[4b] with reaction ampoules made of Teflon and thin-walled glass. The heats of complex formation (q_1) were measured by adding amine solution in the given solvent (*ca.* 0.6 mol dm^{-3}; *ca.* 1 ml) to iodine solution in the same solvent (*ca.* 5×10^{-3} mol dm^{-3}; 90 ml). The heats of solution and of dilution of the amines to the final concentration (q_2) were determined separately. The heat of dilution of the iodine solution to the final concentration was negligible. The molar enthalpies of complex formation were calculated as $\Delta H_c = (q_1 - q_2)/n$, where n is the number of moles of the complex in the solution calculated from the K_c values obtained by the spectroscopic method. The ΔH_c, ΔH_s, and ΔH_d values listed in Tables 2 and 3 are the averages of at least three measurements. The uncertainty limits were calculated as standard deviations of the mean values.

Calculation of K_c Values.—A modified Ketelaar equation accounting for the free iodine absorption[4a] was applied to measured absorbances of every set of solutions containing the

Table 1. Spectral and thermodynamic characteristics of 2-amino- and 3-amino-pyridine(D)–molecular iodine(A)–solvent systems; T 298.2 K [reaction (1)]

Donor	Solvent	$10^{-3}C_D$/mol dm^{-3}	$10^{-4}C_A$/mol dm^{-3}	K_c/dm^3 mol^{-1}	$\varepsilon_{max.}$[a]/dm^3 mol^{-1} cm	$\lambda_{max.}$[a]/nm	$-\Delta H_c$[b]/kJ mol^{-1}	$-\Delta S_c$/J mol^{-1} K^{-1}
2-Aminopyridine	Cyclohexane	0.8—8.0	4.0	273	1 570	412	38.0	81 ± 4[c]
pK_a 6.71	Carbon tetrachloride	2.0—20	2.0	195	1 660	408	33.7	69 ± 4[c]
	Benzene	1.8—18	2.1	148	1 850	399	32.2	78 ± 2
	Chlorobenzene	0.6—8.0	2.2	302	1 820	396	37.9	79 ± 2
3-Aminopyridine	Cyclohexane[d]	0.1—2.0	*ca.* 1	380	1 810	415	37.6	75.2 ± 4[c]
pK_a 6.03	Carbon tetrachloride	0.4—3.8	1.8	292	2 010	407		
	Benzene	0.5—5.0	2.2	260	2 200	398		
	Chlorobenzene	0.3—3.4	2.4	575	2 230	395		
2,4-Dimethylpyridine[e]	Cyclohexane	3.0—20	2.5	364	1 610	420	37.2	80 ± 1
pK_a 6.6	Carbon tetrachloride	3.0—20	2.6	284	1 790	412	34.3	76 ± 1
	Benzene	3.0—20	2.5	228	1 960	402	34.7	76 ± 2
	Chlorobenzene	3.0—20	2.3	575	2 050	399	36.8	85 ± 2

[a] Perturbed iodine band. [b] Spectroscopic method. [c] From spectroscopic ΔH_c value. [d] From ref. 5. [e] From ref. 4*b*.

Table 2. Heats of complex formation, ΔH_c, for molecular complexes of iodine with 2-aminopyridine and 2,4-dimethylpyridine;[4b] heats of transfer of the complexes, [ΔH_{tr} (AD)] and of molecular iodine[7] [ΔH_{tr} (A)] from carbon tetrachloride to benzene and chlorobenzene (from calorimetric data); T 298.2 K

Donor (D)	Solvent	Final concentrations C_D/mol dm^{-3}	 C_A/mol dm^{-3}	$-\Delta H_c$ kJ mol^{-1}	ΔH_{tr} (A)^a kJ mol^{-1}	ΔH_{tr} (AD) kJ mol^{-1}
2-Aminopyridine	Carbon tetrachloride	*ca.* 10^{-3}	2.0×10^{-4}	33.7 ± 3^b	0	0
	Benzene	4.1×10^{-3}	5.7×10^{-3}	35.8 ± 0.5	-6.5	-13
	Chlorobenzene	7.0×10^{-3}	4.0×10^{-3}	37.6 ± 0.5	-4.4	-12
2,4-Dimethylpyridine	Carbon tetrachloride	4.0×10^{-2}	5.5×10^{-3}	36.6 ± 0.5	0	0
	Benzene	5.5×10^{-2}	5.5×10^{-3}	36.0 ± 0.3	-6.5	-4
	Chlorobenzene	5.5×10^{-2}	5.5×10^{-3}	41.0 ± 0.1	-4.4	-9

[a] The errors in ΔH_s of iodine for CCl_4, benzene, and chlorobenzene are ± 0.8, ± 0.2, and ± 0.2 kJ mol^{-1}, respectively. [b] From spectroscopic measurements.

Table 3. Heats of solution (ΔH_s) and heats of transfer [ΔH_{tr} (D)] of 2-aminopyridine, 3-aminopyridine, and 2,4-dimethylpyridine[4b] from carbon tetrachloride to benzene and chlorobenzene; T 298.2 K (calorimetric method)

Base	Solvent	Final conc. mol dm^{-3}	ΔH_s kJ mol^{-1}	ΔH_{tr} (D) kJ mol^{-1}
2-Aminopyridine	Carbon tetrachloride	8.1×10^{-3}	29.7 ± 0.9	0
	Benzene	9.0×10^{-3}	25.3 ± 0.3	-4.4 ± 1.2
	Chlorobenzene	8.1×10^{-3}	25.9 ± 0.2	-3.8 ± 1.1
3-Aminopyridine	Carbon tetrachloride	10.5×10^{-3}	32.0 ± 0.9	0
	Benzene	8.1×10^{-3}	24.9 ± 0.5	-7.1 ± 1.4
	Chlorobenzene	8.7×10^{-3}	26.8 ± 0.4	-5.2 ± 1.3
2,4-Dimethylpyridine[4b]	Carbon tetrachloride	3.8×10^{-2}	-1.34 ± 0.08	0
	Benzene	5.5×10^{-2}	0.49 ± 0.01	$+1.83 \pm 0.1$
	Chlorobenzene	5.5×10^{-2}	-1.13 ± 0.01	$+0.21 \pm 0.1$

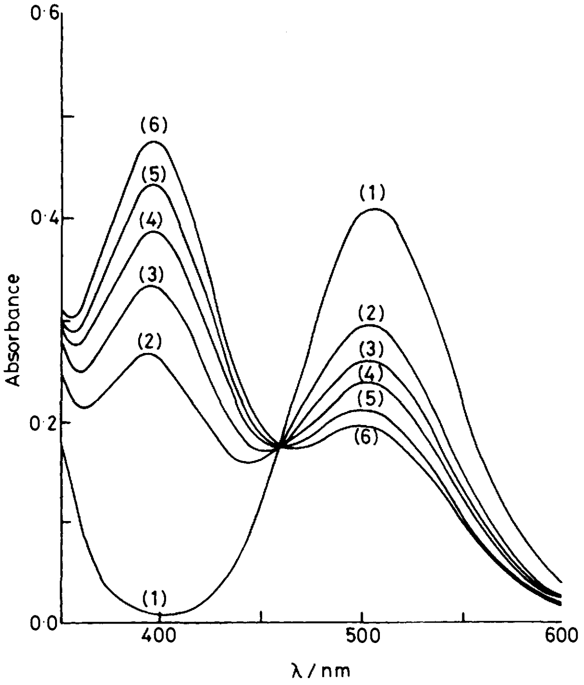

Figure 1. Electronic spectra of 2-aminopyridine–molecular iodine–chlorobenzene solutions at 298.2 K; [I_2] = 2.292×10^{-4}; [2-APy] $\times 10^3$/mol dm^{-3} = 0 (1), 0.5986 (2), 0.8979 (3), 1.197 (4), 1.496 (5), 1.796 (6); l = 2 cm.

same iodine concentration and various amounts of donor (at least five solutions per set). The values given in Table 1 represent the averages of at least two independent sets of solutions. The standard deviations are within $\pm 5\%$. For the 2-APy complexes the ΔH_c values were calculated from the temperature dependence of lg K_c (two independent series; four points in the series; temperature range 285—301 K).

Results and Discussion

Thermodynamic Characteristics of Complex Formation between Aminopyridines and Iodine.—The measured electronic spectra of all the systems investigated show a pattern typical of molecular iodine–amine complexes with clear isosbestic points, when measured at the concentrations given in Table 1 (Figure 1). This suggests that there are only two forms of iodine in equilibrium: a molecular complex with the amine, and the I_2 molecule solvated by the medium [equation (1)]. This means

$$APy + I_2 = APyI_2 \qquad (1)$$

that in all solutions investigated the aminopyridines act as one-site donors towards iodine. Additional evidence for only one type of complex in the solutions may be inferred from the agreement of the K_c values calculated for different analytical wavelengths ($\lambda_{max.}$, $\lambda_{max.} \pm 3$ nm, and $\lambda_{max.} \pm 6$ nm). The spectral position of the perturbed iodine band and the values of the calculated equilibrium constants are similar to those found for iodine–2,4-dimethylpyridine complexes, which suggests that complexation occurs through the ring nitrogen. This conclusion is supported by the steric effect observed for 2-aminopyridine as a donor towards iodine: Table 1 shows that K values for 2-

aminopyridine are much lower than those for the weaker donor, 3-aminopyridine.

The spectra remained constant (±0.15%) for at least 2 h, though 3-APy–I_2 solutions showed optical instability after longer periods and when measured at higher donor concentrations. This fact, caused probably by additional reactions in the system,[5] made measurements of ΔH_c values for 3-APy complexes dubious.

(a) *Stability Constants*, K_c.—The K_c values calculated from measurements on the perturbed iodine band (see Experimental section) are listed in Table 1. The value obtained for the 2-aminopyridine complex in cyclohexane agrees very well with that reported[5] (280 mol dm^{-3}). For comparison, Table 1 also contains K_c values obtained[4b] for a similar system with a pyridine base of comparable strength, *viz.* 2,4-dimethylpyridine (pK_a 6.6). The K_c values for 2-aminopyridine in all the solvents are lower than those for 3-aminopyridine complexes, a fact which can be easily explained by steric hindrance by the α-substituent. A comparison of the data for all three donors shows, however, that K_c values do not follow strictly the order of basicities of the amines as measured by their pK_a values (the steric effects of the *ortho*-NH_2 and -CH_3 groups should be the same[8]). It is interesting that the effect of solvent on the thermodynamic stability of the complexes of both aminopyridines with iodine shows the same pattern as found for the alkyl- and chloro-substituted pyridines and quinolines studied previously,[2] with the K_c decreasing in the order chlorobenzene > cyclohexane > carbon tetrachloride > benzene. This sequence does not correlate with any of the known solvent characteristics, though there is a roughly rectilinear decrease in lg K_c with Hildebrandt's solubility parameter, σ, or the polarity parameter $(\varepsilon - 1)/(2\varepsilon + 1)$, for the last three solvents. Thus the iodine–pyridine derivative complexes represent an intermediate case between strong polar complexes, stabilized by increasing polarity of the medium,[9] and less polar weak complexes, the stability constants of which, as a rule, decrease in more polar solvents[10] as a result of squeezing out of the solvent molecules from the co-ordination spheres of donor and acceptor in the course of complex formation. The fact that chlorobenzene does not fit such correlations does not, however, necessarily imply that its interactions with the solutes are mainly nonspecific and different in character from those exerted by benzene as a solvent; both entropic and enthalpic terms contribute to ΔG values and the enthalpies of solute–solvent interactions are comparable for the two solvents (see later). We consider that the relatively high $\Delta G_c°$ values for chlorobenzene reflect an increase in the dipole moment after complex formation with respect to the constituents, which manifests itself as increased stabilization of the complex in a more polar medium (the dielectric permittivities of chlorobenzene and benzene are 5.62 and 2.27, respectively).

The similarity in the effects of solvent on K_c values for various members of the pyridine family, irrespective of basicity, substituent, and steric hindrance, may be clearly seen from the plots of lg K_c for each member[2] *vs.* the lg K_c for one of the donors chosen as a reference base (Figure 2).The approximately equal slopes of the rectilinear plots for every donor in the Figure indicate that the difference in $\Delta G_c°$ of complex formation with the same donor in two given solvents, s_1 and s_2, is approximately constant, independent of the donor [equation (2)]. This in turn may suggest that the specific solvation of the

$$\Delta G_D° (s_1) - \Delta G_D° (s_2) = \text{const.} \qquad (2)$$

amines involving the lone pair on the ring N atom is comparatively weak and dominated by other factors, *e.g.* local dipolar forces; if such interactions were strong the displacement of the solvent co-ordinated to the unhindered donor site in the course of complex formation would cause the *ortho*-substituted donors to deviate from the common dependence of K_c on solvent.

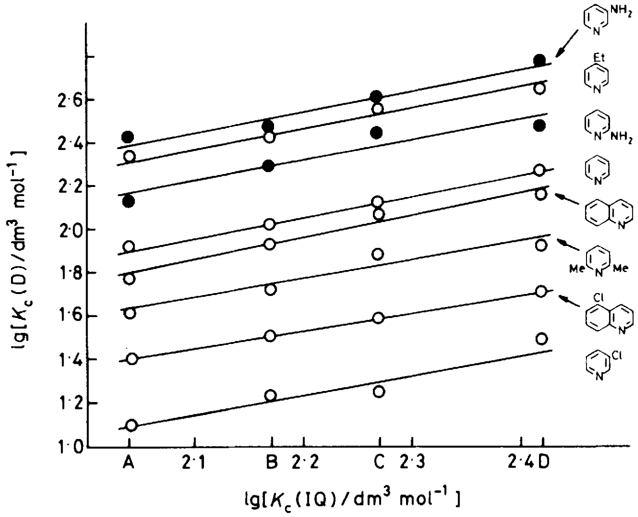

Figure 2. Plots of lg K_c for iodine complexes with pyridines and quinolines and of lg K_c (D) *vs.* lg K_c of isoquinoline complex in the same solvent, lg K_c (IQ); T 298.2 K; solvents benzene (A), carbon tetrachloride (B), cyclohexane (C), chlorobenzene (D); aminopyridines (●); alkyl- and chloro-substituted pyridines and quinolines[2] (○)

(b) *Enthalpies*.—The vast majority of published ΔH_c values for donor–acceptor complexes has been obtained from spectroscopic measurements using the dependence of lg K_c on T. Even the best data of this kind may involve an error of at least 2 kJ mol^{-1}.[11] Thus the calorimetric ΔH_c values should be more reliable, especially for studying solvent effects. Such data are, however, very scarce. Unfortunately the low solubility of the aminopyridines in weakly polar solvents, *e.g.* 3-aminopyridine and 2-aminopyridine in hexane, cyclohexane and carbon tetrachloride, as well as additional reactions which occur, as evidenced by spectrophotometric measurements, at concentrations required for calorimetric measurements ($\geqslant 5 \times 10^{-3}$ mol dm^{-3}), make only few of the ΔH_c values calorimetrically accessible. These are shown in Table 2 together with the data for 2,4-dimethylpyridine, for comparison. The agreement with the spectrophotometric data is reasonable. However, the additional calorimetric data (heats of solution of the donor and iodine, Tables 2 and 3) make it possible to calculate the heats of transfer of the donor–acceptor (DA) complex from carbon tetrachloride to benzene and chlorobenzene by using the thermodynamic cycle [equation (3)]. Though the error in ΔH_{tr}

$$\Delta H_{tr}\,(AD)(s_2 \longrightarrow s_2) = \Delta H_c\,(s_2) - \Delta H_c\,(s_1) + \Delta H_{tr}\,(D) + \Delta H_{tr}\,(A) \qquad (3)$$

(AD) may be greater than that in ΔH_c, it is much smaller than the calculated ΔH_{tr} (AD) values. Thus we may conclude from the data in Table 2 both that the aromatic solvents solvate the complex much more strongly than is the case with carbon tetrachloride, and that the interactions of the complex with benzene and chlorobenzene are of similar magnitude. A comparison of the ΔH_{tr} (AD) values for the two donors 2-aminopyridine and 2,4-dimethylpyridine shows that the complex with the NH_2-substituted donor is better solvated by aromatic solvents. This may be ascribed to H–π bonding involving the acidic hydrogen atoms of the NH_2 group.

(c) *Amine–Amine and Amine–Solvent Interactions.*—There is some difficulty in interpreting the heats of solution of pyridine derivatives in terms of solute–solvent interactions because of their self-association.[12] The relatively high values of ΔH_s for both aminopyridines in all three solvents (as compared with ΔH_s for 2,4-dimethylpyridine) may involve two effects: heats of fusion of the crystalline bases, and amine–amine interactions in the hypothetical pure liquid state. The latter effect, though present in all pure amines as liquids, seems to be particularly strong for the aminopyridines. This conclusion comes from the comparison of their ΔH_s with those for the crystalline 3-cyanopyridine (22.7 ± 0.6, 18.0 ± 0.7, and 18.2 ± 0.3 kJ mol^{-1} for carbon tetrachloride, benzene, and chlorobenzene, respectively[13]) and from spectral studies.[12] Ramish and Puranik[12] reported i.r. spectra for 2-APy in carbon tetrachloride and benzene and for 3-APy in benzene, from which they concluded that the aminopyridines are not fully associated in the solid state and that the extent of self-association in the solution depends on the solvent. The i.r. data are not precise enough for calculation of the dissociation constants, even if we assume that the postulated[12] association scheme is correct. However, the dependence of the absorptivity coefficients of the stretching modes of the bonded and unbonded N–H groups on the concentration strongly suggests that if these groups are responsible for the self-association of the amines, more than 90% of the amines exist in non-bonded form at the concentrations listed in Table 3, and that the degrees of dissociation in different media at the same concentration are similar. This allows us to discuss the heats of transfer of the amines between these solvents in terms of solvent effect only.

The calculated ΔH_{tr} values of the aminopyridines for transfer from carbon tetrachloride to the aromatic solvents (Table 3) reveal that: (i) chlorobenzene and benzene solvate the two amines with similar strength; (ii) the solvation by aromatic solvents is stronger than that by carbon tetrachloride; (iii) the interactions with the aromatic solvents are much stronger for amino derivatives than for 2,4-dimethylpyridine and other alkyl-substituted pyridines.[4b] All these conclusions are consistent with the postulated H–π interactions. These interactions should be much weaker than the H–N(ring) hydrogen bonds which, most probably, cause the aminopyridines to associate. The measured endothermic heats of dilution of the 2-aminopyridine solutions (this work) in benzene (3.4 ± 0.3 kJ mol^{-1} from 0.43 to 4×10^{-3} mol dm^{-3}) and chlorobenzene (5.0 ± 0.2 kJ mol^{-1} from 0.76 to 6×10^{-3} mol dm^{-3}) show that this is really the case.

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